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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,783	06/01/2001	Jingye Liu	CCP-100	4651

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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,783	LIU ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8 and 11-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6, 7, 11-13 and 15* is/are rejected.

7)☒ Claim(s) *5,8,14 and 16-19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

In paper no. 12, applicant amended claims 6, 7 and added new claims 13-19. Claims 1-3, 5-8 and 11-19 are under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1-3, 6, 7, 11, 12 and newly presented claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Funkhouser et al. (US 6,113,912 or 6,180,110 B1, in the alternative) and Chiba-ken et al. (JP 1279843 abstract provided with IDS in paper no. 5) as evidenced by Hollinger et al. (Hepatitis A Virus. *In* B.N. Fields et al. (ed.), Fields Virology, 3rd ed. Philadelphia: Lippencott-Raven Publishers; 1996: 739 and 766-769). Since the limitations presented in claims 13 and 15 do not alter the scope of the rejection, the claims are also rejected for reasons presented for claims 1-3, 6, 7, 11 and 12.

Claim 1 is drawn to formulation comprising a live, lyophilized, attenuated HAV and a stabilizer.

Funkhouser et al. teach a formulation comprising a live, attenuated HAV and a stabilizer, see column 17, lines 10-43 of US 6,113,912 or column 15, line 64 to column 16, line 29 of US 6,180,110 B1, in the alternative.

As applicant points out in the response, neither Funkhouser et al. patent teach lyophilization.

However, Chiba-ken et al. teach obtaining an HAV virus and freeze-drying with a stabilizing agent comprising an amino acid, various sugars, and a gelatinizing agent. One of ordinary skill in the art at the time the invention was made would have been motivated to lyophilize the HAV of either Funkhouser et al. reference to increase storage stability and obtain an HAV vaccine that is quickly soluble when ready to use. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for lyophilizing the HAV of either Funkhouser et al. reference with the method of Chiba-ken et al. because all of the references use HAV vaccines and lyophilizing viruses for vaccine use is conventional practice in the vaccine art. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Alternatively, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate a live HAV in to the formulation of Chiba-ken et al. to administer a replication-competent virus to expose the immune system to all of the expression products to the immune system as the virus replicates. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because the formulation of Chiba-ken et al. comprises all of the components necessary to stabilize virus particles, live or inactivated, for long periods of time.

Although neither Funkhouser et al. reference nor Chiba-ken et al. teach incorporating hepatitis A virus LAI strain into the formulation, all of the references teach that and HAV is suitable. Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to incorporate the live, effective hepatitis A LAI vaccine,

admitted as well known in the instant disclosure on page 2, into the vaccine composition of either Funkhouser et al. reference combined with the formulation of Chiba-ken et al. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Applicant argues that Chiba-ken et al. do not teach using a live vaccine formulation and do not provide a reasonable expectation of success because an inactivated and a live virus have different structural and functional properties.

Applicant's arguments have been fully considered, but are found unpersuasive. The difference between the HAV viruses of either Funkhouser et al. patent or the HAV virus of Chiba-ken et al. is their ability to infect. Contrary to applicant's assertions, the structural elements present in inactivated HAV and live HAV vaccines are the same. Hollinger et al. state that HAV virions have a primary buoyant density of 1.32 to 1.34 g/cm^3 in CsCl and measure 27- to 32-nm in diameter, see page 739. Inactivated HAV virion particles in vaccine compositions have the same structural morphology. The inactivated HAV vaccine particles also induce neutralizing antibodies and protection against challenge, clearly indicating that the viral epitopes required for immune functioning are indistinguishable from live HAV virions. See page 766. Therefore, the structural features of the live HAV viruses of either Funkhouser et al. patent or the inactivated HAV virus of Chiba-ken et al. are indistinguishable. It is maintained that the ordinary artisan would have had a reasonable expectation for combining the lyophilizing and stabilizing the live HAV vaccine of either Funkhouser et al. patent in the composition and method of Chiba-ken et al.

Applicant also asserts before the invention was made, the art did not know how to make a live, attenuated lyophilized HAV vaccine. However, this is clearly not the case, since Funkhouser et al. teach combining stabilizers with the live HAV vaccine formulation, see column 16, lines 17-29 of '110 or column 17, lines 31-43 of '912 and Chiba-ken et al. lyophilizes and stabilizes an HAV vaccine.

Applicant also offers conjectures for why the invention was not invented sooner. However, these hypotheses are irrelevant because they do not address the teachings of Chiba-ken et al. or either Funkhouser et al. reference.

Allowable Subject Matter

Claims 5, 8, 14 and 16-19 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or suggest a formulation comprising all of the ingredients at the recited concentrations.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley

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